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The Forbidden Genetic Code Combinations

Sivashanmugam. P., Lecturer, Biophysical Chemistry,
Department of Bioinformatics, Jamal Mohamed College, Tiruchirappalli – 620020 – India
e-mail: *soundaryanayaki@aol.com*

The proteogenic amino acids tryptophan, cysteine, and methionine have only a single codon for each in the table of universal genetic code. The relative frequency of each of these codons is 1.5625%. Strikingly, the relative distribution of these amino acids in enzymes are also invariably less than 3.0% irrespective of the class and type of the reaction catalyzed. The amino acids other than tryptophan, cysteine and methionine show a variable distribution. One would also find that the following genetic code combinations are not found in nature. There are some hypothetical, predicted, or cloned sequences and proteins in the databases like NCBI. But, none of them are natural.

The list of forbidden genetic code combinations:

1. TGG TGT ATG corresponding to the amino acid combination WCM
2. TGG ATG TGT corresponding to the amino acid combination WMC
3. TGT ATG TGG corresponding to the amino acid combination CMW
4. TGT TGG ATG corresponding to the amino acid combination CWM
5. ATG TGT TGG corresponding to the amino acid combination MCW
6. ATG TGG TGT corresponding to the amino acid combination MCW

Based on these observations, I conclude that nature does not allow the genetic code combinations to occur with equal probability. If the combinations occur equally likely, then one should observe these combinations must occur with the same relative frequency as those of other code combinations. Why nature forbids such combinations is yet to be answered. Is it biophysically restricted or is it a genetic restriction? These are unanswered questions.

One could also make proteins, if possible, with these restricted combinations (either by site directed mutagenesis or by solid state synthesis) and study their biophysical properties. The above observation is purely based on the data available from the NCBI and RCSB.

I like to hear the answer from those having sophisticated labs and full government support to carry out any kind of experiment.